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TOPICAL TOPICS

This issue contains the first of what will be occasional notes in *Medical and Pediatric Oncology* that will appear under the heading ''Topical Topic.'' It is perhaps easier—rather like non-Hodgkin lymphoma—to define them by stating what they are not. They are not designed to be editorials, nor exhaustive reviews of a specific topic, nor expressions of personal experience or opinion. Rather, they will encompass elements of all three.

Leading authorities will provide unsolicited or solicited comments on some aspect within the broad field of cancer, be it laboratory research, clinical management, or epidemiologic investigations that are of current interest and importance. They will be brief, to-the-point expositions that it is hoped will provide the readership of MPO with authoritative guidance and information in an interesting and lively format.

Doctors Donckerwolcke and Coppes address such a matter of importance and current interest in their review of ''Cytotoxic treatment and alterations in kidney function.''

Cytotoxic Treatment and Alterations in Kidney Function

Bone marrow transplantation (BMT) is now recognized as an effective form of therapy for an increasing number of childhood disorders, including immunodeficiencies, storage diseases, leukemia, lymphoma and a variety of solid tumors. The use of cytotoxic drugs prior to BMT and the subsequent use of ablative doses of chemotherapy, sometimes with additional total body irradiation (TBI), in preparation for marrow or stem cell transfusion, induces toxicity in many organs. Although some unwanted renal effects, such as the development of acute renal failure secondary to tumor lysis, are well known, the fact that the kidneys are particularly vulnerable to chemotherapy and irradiation has often been neglected. As a consequence, the presence of chronic renal damage is not often reported and has been mainly related to the use of cisplatin and ifosfamide [1].

In a recent issue of Medical and Pediatric Oncology, Paltzer et al. report on renal function in patients who underwent a BMT [2]. Prior to conditioning therapies, 15% of the patients studied had urinary protein loss, indicative of abnormal glomerular permeability and over 50% had signs of renal tubular dysfunction. Following conditioning therapies, abnormal glomerular permeability was found in 50% of patients while over 75% had signs of tubular damage. First and foremost, these findings contradict prior reports which suggest that alterations in renal function are not common in patients having undergone a BMT [3]. This could be explained by the fact that Paltzer et al., did not rely on serum creatinine levels to determine renal functional abnormalities. Previous studies have demonstrated that serum creatinine levels are a poor indicator of kidney damage in patients treated for malignancies [4], an observation confirmed in this study. The significance of the observation reported here, is that the screening test used (proteinuria for glomerular function) shows renal damage following treatment for cancer prior to conditioning therapy, while further damage is demonstrated following conditioning therapy. Unfortunately, the investigators were unable to determine a reliable glomerular filtration rate immediately following conditioning therapy and therefore the clinical significance of their findings cannot be assessed.

While the majority of children demonstrated significant proteinuria and proximal tubular toxicity following BMR conditioning, it remains to be determined whether these changes are permanent, progressive or transient. The authors indicate that they intend to report long term follow-up findings and we look forward to their data.

Based on this and other reports, we advocate that the renal function of children who are treated for cancer should be screened by measurement of urinary protein excretion (for glomerular abnormalities) and clearances of l-α microglobulin or β-NAG (for tubular function). If these screening tests yield abnormal values, the clinical relevance of the presumed glomerular abnormality can be measured by a single sample clearance study of iohexol or a radioactive indicator, while assessment of

fractional excretion of filtered sodium and reabsorption of phosphate by collection of a single blood and urine sample will help assess the clinical importance of tubular abnormalities [5].

What can we do about renal damage due to therapy? We believe it is time to start considering new therapeutic interventions to reduce renal damage in patients receiving cytotoxic therapy (with or without irradiation) and nephrotoxic drugs, such as aminoglycosides, vancomycin, amphotericin B and cyclosporin A. The simplest approach includes adequate hydration: saline infusions are commonly used to reduce renal toxicity of cisplatin, ifosfamide and amphotericin B. In addition however, several drugs come to mind. For example, disulfiram, a thiol compound, which has been shown to protect the renal tubule by chelation of cisplatin and its active metabolites [7] and erythropoietin which, when administered following cisplatin induced acute renal failure, has been shown to stimulate renal tubular cell recovery [8]. To us, the amino acid glycine seems an intriguing compound to test in this setting. In a recent study, oral glycine administered to rats treated with ifosfamide showed a protective effect on tubular function [9]. Human testing has thus far not been reported and the exact mechanism by which glycine protects the renal tubular cells has yet to be described. It is conceivable that glycine will also be helpful to prevent tubular damage by other cytotoxic drugs. We are therefore eagerly awaiting additional information on this and other renal sparing' approaches, although the study by Paltzer et al. suggests that a lot still needs to be done to increase our awareness of the magnitude of the problem.

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